

New pyrrolidone, imidazolone, furanone or thiophene derivatives

Patent Number: DE19626701

Publication

date: 1998-01-08

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Requested

Patent: ☐ DE19626701

Application

Number: DE19961026701 19960703

Priority Number

(s): DE19961026701 19960703

IPC

Classification: C07D233/76; C07D403/12; A61K31/47; A61K31/415; A61K31/44; A61K31/425; A61K31/505; C07K5/06; C07D521/00

EC

Classification: C07D233/96, C07D403/12, C07D471/10

Equivalents:

Abstract

5-Membered azacyclic derivatives (I) and their salts are new. W = C(R<16>)-D-B-A-R<1> (a), C=C(R<16>)-D-B-A-R<1> (b) or a group of formula (c) or (d); the ring of formula (e) is saturated or partly or fully unsaturated, and optionally contains 1 or 2 N, O and/or S atoms and is optionally mono-, di- or trisubstituted by R<16> or mono- or disubstituted by =Q; Y = CQ or CH₂; Z = N(R<0>), Q or CH₂; A = bond, 1-8C alkanediyl, CR<2>=NNR<2>, NR<2>CQNR<2>, QCQ'NR<2>, NR<2>S(O)nNR<2>, OS(O)nNR<2>, S(O)nNR<2>, 3-12 cycloalkanediyl, C?=C, NR<2>CO, CONR<2>, NR<2>CO-5-14C arylene, O, S(O)n, 5-14C arylene, CO, CO-5-14C arylene, NR<2>, NR<2>SO₂, OCO, COO, N=CR<2>, CR<2>=N, CR<2>=CR<3> or S(O)n-5-14C arylene (all optionally substituted by NR<2> and/or by 1 or 2 1-8C alkanediyl); Q, Q' = O or S; B = bond, 1-8C alkanediyl, 5-10C arylene, 3-8C cycloalkanediyl, C?=C, NR<2>, CO, CONR<2>, NR<2>CO, NR<2>-CQ-NR<2>, OCO, COO, SO, SO₂, SONR<2>, SO₂NR<2>, NR<2>SO, NR<2>SO₂, Q or CR<2>=CR<3> (all optionally mono- or disubstituted by 1-6C alkanediyl) or a divalent residue of a 5-6 membered saturated or unsaturated ring containing 1 or 2 N atoms (optionally mono- or disubstituted substituted by 1-6C alkyl or =Q); D, F = bond, 1-8C alkanediyl, 5-10C arylene, Q, NR<2>, CONR<2>, NR<2>CO, NR<2>CQNR<2>, OCO, COO, CQ, SO, SO₂, SO₂NR<2>, NR<2>SO, NR<2>SO₂, CR<2>=CR<3>, C?=C, CR<2>=NNR<2>, N=CR<2>, CR<2>=N or CHOH (all optionally mono- or disubstituted by 1-8C alkanediyl, CR<2>=CR<3> or 5-6C arylene); E = bond, 1-6C alkanediyl, 2-6C alkanediyl, 2-6C alkynediyl, phenylene, phenylene-1-3C alkanediyl or 1-3C alkanediyl-phenylene; G = CR<4>-R<5>-(CR<6>-R<7>)p(CH₂)qR<10>; L = C(R<16>) or N; R<0> = H, 1-8C alkyl (optionally substituted by 3-12C cycloalkyl or 5-14C aryl), 1-8C alkylcarbonyl, 3-12C cycloalkyl-carbonyl, (3-12C cycloalkyl- or 5-14C aryl-substituted) 1-6C alkylcarbonyl, 5-14C aryl-carbonyl, 3-12C cycloalkyl or 5-14C aryl (where all alkyl are optionally substituted by 1 or more F); R<1> = NR<2>CR<2> (=NR<2>), C(=NR<2>)NR<2>R<3>, NR<2>C(=NR<2>)NR<2>R<3>, or a 4-14 membered mono- or polycyclic optionally aromatic ring (optionally containing 1-4 N, O and/or S and optionally substituted by R<12>-R<15>); R<2>, R<3> = H, 1-10C alkyl (optionally substituted by 1 or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkyl, 5-14C aryl, 5-14C aryl-1-8C alkyl, NH₂; NR<9>OR<8>, R<9>OR<8>, R<9>COOR<8>, R<9>-5-14C aryl-R<8>, R<9>N(R<8>)₂, R<9>-NR<8>-(1-8C hydroxyalkyl), R<9>CON(R<8>)₂, R<9>NR<8>COR<8>, R<9>COR₈, C(=NR<8>)N(R<8>)₂; NR<8>C(=NR<8>)N(R<8>)₂ or (1-18C alkyl)-COO-1-6C alkoxycarbonyl; R<4>-R<7> = H, F, OH, 1-8C alkyl, 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkyl, R<9>QR<8>, R<9>OCOR<8>, R<9>COOR<8>, R<9>-5-14C aryl-R<8>, R<9>N(R<2>)R<8>, R<9>N(R<8>)₂, R<9>OCONR<8>R<2>, R<9>N(R<2>)S(O)nR<8>, R<9>NR<2>COQR<8>, R<9>NR<2>COR<8>, R<9>N(R<2>)CON(R<2>)R<8>, R<9>N(R<2>)S(O)

$nNR<2>R<8>$, $R<9>S(O)nR<8>$, $R<9>NR<2>COSR<8>$, $R<9>COR<8>$, $R<9>CONR<2>R<8>$ or $R<9>S(O)nNR<2>R<8>$; $R<8> = H$, 1-8C alkyl (optionally substituted by 3-12C cycloalkyl or 5-14C aryl), 3-12C cycloalkyl or 5-14C aryl (where all alkyl are optionally substituted by 1 or more F); $R<9> =$ bond or 1-8C alkanediyl; $R<10> = CQR<11>$, $S(O)nR<11>$, $P(O)nR<11>$ or a 4-8 membered saturated or unsaturated heterocycle containing 1-4 N, O and/or S atoms; $R<11> = OH$, 1-8C alkoxy, 5-14C aryl-1-8C alkoxy, 5-14C aryloxy, 1-8C alkylcarbonyloxy-1-4C alkoxy, 5-14C aryl-1-8C alkylcarbonyloxy-1-4C alkoxy, NH_2 , mono- or di-1-8C alkylamino, 5-14C aryl-1-8C alkylamino, 1-8C dialkylaminocarbonylmethoxy, 5-14C aryl-1-8C dialkylaminocarbonylmethoxy, 5-14C arylamino or a D- or L-amino acid; $R<12>-R<15> = H$, 1-10C alkyl (optionally substituted by one or more F), 3-12C cycloalkyl, 3-12C cycloalkyl-1-8C alkyl, 5-14C aryl, 5-14C aryl-1-8C alkyl, NH_2 , $R<9>OR<8>$, $R<9>COOR<8>$, $R<9>N(R<8>)_2$, $R<9>-5-14C\ aryl-R<8>$; $R<9>-NR<2>$ (1-8C hydroxyalkyl), $R<9>CON(R<2>)R<8>$, $R<9>N(R<2>)COR<8>$, $R<9>COR<8>$, $NR<2>C(=NR<3>)-NR<2>R<3>$, $C(=NR<2>)NR<2>R<3>$ or Q; or 2 of $R<12>-R<15>$ which are adjacent form $-OCH_2O-$, $-OCH_2CH_2O-$ or $-OC(CH_3)_2O-$; $R<16> = H$, 1-10C alkyl optionally substituted by 1 o

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DEUTSCHES
PATENTAMT

⑫ Offiziell eingetragene
⑩ DE 196 26 701 A 1

⑳ Aktenzeichen: 196 26 701.3
㉑ Anmeldetag: 3. 7. 98
㉒ Offenlegungstag: 8. 1. 98

㉓ Int. Cl.⁶:
C 07 D 233/76
C 07 D 403/12
A 61 K 31/47
A 61 K 31/415
A 61 K 31/44
A 61 K 31/425
A 61 K 31/505
C 07 K 5/08
// C 07 D 521/00
(C 07 D 403/12, 233:76,
249:08)

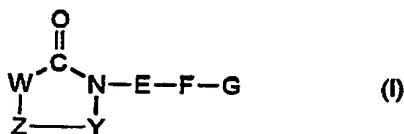
DE 196 26 701 A 1

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㉖ Neue Inhibitoren der Knochenresorption und Vitronectinrezeptor-Antagonisten

㉗ Gegenstand der vorliegenden Erfindung sind 5-Ring-Heterocyclen der allgemeinen Formel I,



in der E, F, G, W, Y und Z die in den Patentansprüchen angegebenen Bedeutungen besitzen, ihre Herstellung, ihre Verwendung als Heilmittel und sie enthaltende pharmazeutische Zubereitungen. Die Verbindungen der Formel I wirken insbesondere als Vitronectinrezeptor-Antagonisten und Inhibitoren der Knochenresorption durch Osteoclasten.

DE 196 26 701 A 1